REMARKS

Reconsideration is requested.

The claims have been amended, without prejudice, to obviate the objection to claims 26-39 with regard to the recitation of sequence identifiers in the claims. Entry of the Amendment and withdrawal of the objection of the claims is requested.

The claims have been amended, without prejudice, to obviate the Section 112, second paragraph, rejection, of claims 32-39. Entry of the Amendments and withdrawal of the Section 112, second paragraph, rejection of claims 32-39 are requested.

The claims have been amended, without prejudice, to obviate the Section 112, second paragraph, rejection of claims 31 and claims 32-39, dependent therefrom. Entry of the Amendments and withdrawal of the Section 112, second paragraph, rejection of claim 31, and claims 32-39 dependent therefrom, are requested.

The Section 112, first paragraph "enablement", rejection of claims 29-39 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

The Section 112, first paragraph "written description", rejection of claims 29-30 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

The Section 112, first paragraph "written description", rejection of claims 31-39 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

The rejections are being treated here together as the issues and arguments of the Examiner appear to be similar in rejecting the noted claims in the separate sections

of the Office Action of July 8, 2004. The Examiner is requested to advise the undersigned in the event the Examiner's basis for the rejections have been misunderstood or misinterpreted.

Initially, the applicants appreciate the Examiner's acknowledgement that the specification is "enabling for a polynucleotide with SEQ ID NO:1 encoding an exzyme of SEQ ID NO:2 having amidohydrolase activity and [being] capable of hydrolyzing R-3,3,3-trifluoro-2-hydroxy-2-methylpropionamide of Formula VI". See, page 3 of the Office Action dated July 8, 2004.

The applicants submit however that the claims are supported by an enabling disclosure which demonstrates that the applicants were in possession of the claimed invention at the time the application was filed, and consideration of the following in this regard is respectfully requested.

The applicants believe that the Examiner has focused, with some redundancy, on the issue of providing enablement and written description for all possible nucleotide sequences fulfilling the requirements of, for example, claim 26.

The applicants acknowledge, with appreciation, the Examiner's apparent acceptance of the availability of, and advanced level of skill in the art with, both amidase enzyme assays methods and methods for random mutagenesis of nucleotide sequences. The Examiner appears to believe however that, even with this advanced level of skill in the art, the scope of screening work required in random mutagenesis would be an "undue" amount of experimentation. The Examiner's concerns and requirements for "predictability" appear to be unwarranted and misplaced, and, to some extent, contrary to the power and expected use of mutagenesis by those of ordinary skill in the art.

In the applicants opinion, the Examiner's apparent requirement for "predictability" implies that rather than choosing a random mutagenesis approach (which itself is deemed enabled), the Examiner only deems the completely opposed, rational or targeted approach promising for foreseeably successful, and hence, according to the Examiner, "routine" experimentation. The applicants respectfully submit however that the very idea of random mutagenesis in protein engineering is to avoid the pitfalls of being dependent on the alleged accuracy of a pre-determined, theoretical model on structure-activity relationship (SAR) for a given enzyme. Such models are limited in nature by the current understanding of protein structure, which the Examiner himself cites as the yet unsolved protein folding problem (see, page 5 of the Office Action date July 8, 2004, Ngo et al. The protein folding problem and Teritary Structure Prediction). One of ordinary skill in the art will appreciate that while an amino acid sequence determines protein folding, experimental rather than theoretical modeling approaches are needed for 3-D structure determination. Predictions, if any, are computed on empirical scaffold structure data collected and suffer from an inherent margin of error. Protein folding is far from being accurately modeled at present.

However, the applicants believe that consideration of the "Wands" factors, cited by the Examiner, requires a conclusion that the presently claimed invention is supported by an enabling disclosure which adequately demonstrates that the applicants were in possession of the claimed invention at the time the application was field.

The Examiner is urged to appreciate in this regard that it is not only the quantity of experimentation necessary (item 1), but absent specific working examples or guidance in the specification (items 2,3), the nature of the invention and the state of the art in the field to the extent this allows of reproducibility (items 5-7).

The nature of the invention, due to the above-described issue of insufficient understanding of protein folding, is such that it is difficult to anticipate and describe at a structural level all functional variants. Due to the hybridization requirement of the claims, the claimed sequence at least have a considerable degree of homology, stringency amounting to an estimated 80% homology at the DNA sequence level.

Further, the Examiner appears to overlook the fact that the use of random mutagenesis approaches for protein engineering have been used routinely and have been perfected at the time of the present invention, in a way that considerably, and in a reliable, foreseeable manner reduced and streamlined the effort required for successful, routine experimentation.

The DNA shuffling or DNA reassembly approach is a random, function-only-based screening method and its outstanding success has been amply described by different groups and in different methodological versions prior to the priority date of the present invention, e.g. in WO 98/42728, WO 9 7/35966, WO 97/20078, WO 9 8/41622 demonstrating straight forward creation of functional, improved enzyme variants; and WO 98/42832, WO 98/01 581, US 5811238, US 5773221 allowing for random sampling of e.g., amidases of different source rather than starting from a single sequence.

The Examiner is urged to see, for example, WO 98/42728 (copy attached and listed on the attached PTO 1449 Form) as a concise example of a suitably evolved/randomized biocatalyst from a single starting gene sequence. The method did not require undue experimentation for conducting several rounds of screening and selection. Most notably, the DNA shuffling approach is inherently based on the principle of DNA hybridization.

The claims are submitted to be supported by an enabling disclosure which adequately describes the claimed invention. Withdrawal of the Section 112, first paragraph, rejections is requested.

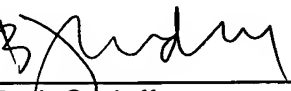
Copies of the above cited evidentiary literature is attached and listed on a PTO 1449 Form, the return of an executed copy of which is requested, pursuant to MPEP § 609. See, MPEP § 609(III)(C(3)).

Entry of the above amendments is requested to, at a minimum, reduce the issues for appeal.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: 

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